REMARKS

The foregoing amendments and the following remarks are submitted for entry and consideration in response to the communication dated October 6, 2006.

Status of the Claims

Claims 14-17 are pending in the application. Claims 14 and 15 have been amended and new claims 33-36 are presented in order to more particularly point out and distinctly claim that which Applicants regard as the invention. With respect to all amendments and canceled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and, moreover, has not acquiesced to any rejections and/or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications. No new matter is added by the amendment of the claims or in the newly presented claims.

Support for the amended and newly presented claims can be found generally through Applicants' Specification. In particular, Applicants point to the Specification, including at page 54-55, page 226 lines 11-14, page 233 lines 17-21, page 235 lines 6-9, Example 12 and Example 18 for support for the specific language of amended claims 14 and 15. New claims 33-36 are supported generally in the Specification, and particularly including at pages 18 and 19, page 161 lines 10-20, Tables 8 and 9 and antibody MC-813-70 which binds SSEA4.

The Double Patenting Rejections

Applicants acknowledge and thank the Examiner for withdrawing the provisional rejection of claims 14-17 under the judicially created doctrine of obviousness-type double patenting over claims 14-17 of copending Application Serial No. 11/029,763 ("the '763 Application")

The Examiner maintains his provisional rejection of claims 14-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-17 of copending Application Serial No. 10/443,663 ("the '663 Application"). In as much as this

rejection is provisional, Applicants acknowledge this rejection and recognize it as provisional at present. The claims in the '663 Application are directed to isolated pluripotent embryonic-like stem cells and claims 14-17 have been cancelled without prejudice. The instant claims, however, are directed to isolated pluripotent embryonic-like stem cells, genetically engineered to express a gene or protein of interest. Without prejudice, Applicants respectfully assert that claims to genetically engineered pluripotent embryonic-like stem cells can be deemed patentably distinct from the isolated stem cells. This is supported by the US PTO's actions in the priority co-pending application USSN 09/404,895, of which the cited '663 Application is a continuation. In the restriction requirement of the 09/404,895 application, restriction was required between Group I, directed to claims 1-13 and 32, drawn to pluripotent stem cells and Group IV, directed to claims 14-17 and 26, drawn to genetically modified pluripotent stem cells. The inventions were deemed by the US PTO Examiner because the "products of Inventions I and IV are materially different products (cells and gene-modified cells) with regard to structure and function, and which can further be used in materially different methods". Applicants respectfully request that the provisional double patenting rejection over Application Serial No. 10/443,663 be withdrawn.

The 35 U.S.C. 112, First Paragraph, Rejection

Claims 14-17 are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This rejection is set out as a new matter rejection, the Examiner maintaining that the recitation "and do not give rise to functional gametes" is considered new matter because there is no description in the Specification for a pluripotent embryonic-like stem cell that does not give rise to functional gametes. In conjunction with this rejection, again to the extent that the Examiner asserts that claimed compositions and/or methods are not described in the instant disclosure, the Examiner maintains his rejection of claims 14-17 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the Specification as to enable the skilled artisan to make and/or use the invention. The Examiner argues that the art shows that pluripotent cells have the capability to produce functional gametes. Applicants respectfully and strongly disagree with this assertion and further submit that the Specification provides support for and describes pluripotent embryonic-like stem cells, which by definition and in character are not totipotent cells and

thereby do not give rise to functional gametes. In addition, the Specfication, particularly when combined with the significant skill and knowledge of the skilled artisan, enables the skilled artisan to make and/or use the invention and the claimed genetically engineered stem cells.

Embryonic stem cells can give rise to functional gametes and are, therefore totipotent, being capable of contributing to the germ line. Embryonic stem cells can also form cells of any of the ectodermal, endodermal, or mesodermal lineages. The pluripotent embryonic-like stem cells of the invention are pluripotent and NOT totipotent. A pluripotent cell, by nature and recognized definition, is not totipotent. A totipotent cell, by nature and recognized definition, is a stem cell capable of forming every type of body cell, including both somatic cells and gametes. While a totipotent cell has all the differentiative capabilities of a pluripotent cell and more (being also able to form gametes, etc.), a pluripotent cell has only a subset of or certain of the differentiative capacities of a totipotent cell. A pluripotent cell is more limited than a totipotent cell. The Specification teaches, including at page 3, lines 29-31, that embryonic stem cells are "totipotent", giving rise to all somatic lineages as well as functional gametes. In contrast, the claimed "pluripotent" embryonic-like stem cells are pluripotent. Applicants have earlier provided evidence, a declaration of inventor Dr. Henry E. Young stating and evidencing that the PPELSCs have not been demonstrated to form gametes. In fact, as established in the Declaration, attempts by the inventor to identify the formation of gametes from the pluripotent embryonic-line stem cells of this invention, at the time of filing and subsequent to the date of filing, have been unsuccessful. The inventor has, however, independently identified a distinct population of stem cells, BLSCs, capable of giving rise to all somatic lineages as well as functional gametes, and established that the assays applied to PPELSCs to evaluate formation of gametes, which generate negative results when screening PPELSCs give positive results with the BLSCs. Applicants PPELSCs are NOT totipotent, and do not give rise to functional gametes.

In the interest of facilitating prosecution and without prejudice to any further or continued prosecution, Applicants have above amended the claims, particularly 14 and 15, to further characterize and indicate identified and described differences between the pluripotent embryonic-like stem cells of the instant invention and other stem cells, including embryonic stem cells or primordial germ cells. Applicants respectfully submit that the claims as presented and amended meet the written description requirement and are fully enabled by the specification.

In view of the foregoing remarks and the above amendments, Applicants submit that the Examiner's 112, first paragraph, rejections are obviated and should be withdrawn.

The §102 Rejections

The Examiner has maintained his rejection of claims 14-16 under 35 U.S.C. 102(b) as being anticipated by Capecchi et al [Scientific American 270(3): 34-41 (1994)]. Capecchi teaches the inactivation of target genes by homologous recombination and the insertion of a *neo* resistance gene, which serves as a positive selection marker, in mouse ES cells. The Examiner again asserts that the Capecchi cells fulfill the limitations of the instant claims because they are transfected, isolated, pluripotent cells which can differentiate into cells from all three germ layers, and do not give rise to functional gametes. Applicants respectfully disagree and again assert that Capecchi et al does not anticipate claims 14-16. Applicants again argue that totipotent cells, including the ES cells utilized and described in Capecchi, can give rise to gametes by definition, where the pluripotent embryonic-like stem cells of Applicants cannot. Capecchi describes targeted gene replacement in mice which requires the germ line transmission of the target via ES cells. Also, Applicants underscore that the claimed ELSCs when grown under inducing conditions as a population of isolated cells do not form gametes, as further evidenced by the inventor's declaration previously submitted. ES cells are totipotent and can form gametes, while pluripotent embryonic-like stem cells of this invention are pluripotent, not totipotent, and cannot form gametes. This is a distinction and difference in fact. The Capecchi reference required germ line transmission of the transfected ES cells. The PPELScs of Applicants could not be used in the Capecchi method to replace genes in progeny mice because they lack the capacity for germ-line transmission, cannot form gametes and are not totipotent. Applicants further point out that the claims have above been amended to more clearly and fully set out the characteristics of the PPELSCs and distinctions with other stem cells, including ES cells and PGCs. The claims as amended set out several aspects of distinction between the PPELSCs of Applicants and ES cells, including the cells of Capecchi et al. The instantly described and claimed cells are not derived from embryonic tissue and are not totipotent, as previously detailed and argued. In addition, while ES cells are recognized as spontaneously differentiating, forming disorganized and heterogenous gatherings of cells in culture, and

forming teratomas (tumors) in animals, the PPELSCs of applicants do not spontaneously differentiate, remaining quiescent in serum-free medium and in the absence of an induction agent, and also do not form tumors in an animal. Applicants PPELSCs are not taught or anticipated by the ES cells of the Capecchi et al reference, totipotent ES cells do not anticipate a pluripotent cell – they are distinct in character and differentiative capacity.

The Examiner maintains his rejection of claims 14-16 under 35 U.S.C. 102(b) as anticipated by Piedrahita et al [Biol of Reprod 58:1321-1329 (1998)], which teaches the generation of transgenic porcine chimeras using primordial germ cells (PGCs)-derived colonies. The Examiner asserts that Piedrahita et al anticipates the claimed invention because the PGCs they teach are capable of differentiation into the three germ layers. Applicants again respectfully submit that the Piedrahita et al cells are absolutely distinct from the pluripotent embryonic-like stem cells of the instant Application. Piedrahita teaches that the chimeric cells contributed to the germ line. The Examiner asserts that although Piedrahita suggests that some of the PGCs may have germline transmission, Piedrahita provides evidence that the cells also could not contribute to the germline in certain chimeric animals. Applicants submit that the technology and laboratory techniques involved in generating transgenic chimeras are complex and imperfect and not every single cell or every single mouse is successfully implanted or successfully transmitted. However, without question, the PGCs of Piedrahita, similar to ES cells, are totipotent, forming cells from all three germ layers – ectoderm, endoderm, and mesoderm – and forming gametes to contribute to the germ line. Whether the scientific techniques are imperfect or every cell does not contribute to germ line is not relevant in this instance. Distinct from PGCs and ES cells, the pluripotent embryonic-like stem cells of the instant Application, in contrast, differentiate to cells derived from all of the endodermal, ectodermal and mesodermal lineages, but cannot form gametes and thus do not and cannot contribute to the germ line. The PPELSCs do not possess all the capabilities of the Piedrahita PGCs. The cells of the instant invention cannot be used in Piedrahita's methods because they cannot contribute to the germline and cannot be used to generate transgenic progeny animals. Applicants further point out that the claims have above been amended to more clearly and fully set out the characteristics of the PPELSCs and distinctions with other stem cells, including ES cells and PGCs. The claims as amended set out several aspects of distinction between the PPELSCs of Applicants and ES cells, including the

cells of Capecchi et al. The instantly described and claimed cells are not derived from embryonic tissue and are not totipotent, as previously detailed and argued. In addition, while ES cells are recognized as spontaneously differentiating, forming disorganized and heterogenous gatherings of cells in culture, and forming teratomas (tumors) in animals, the PPELSCs of applicants do not spontaneously differentiate, remaining quiescent in serum-free medium and in the absence of an induction agent, and also do not form tumors in an animal. The cells of the Piedrahita et al reference are distinct from and do not teach or anticipate the PPELSC stem cells identified and claimed by Applicants.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's 102 rejections are obviated and should be withdrawn.

The §103 Rejections

The Examiner has again maintained his rejection of claims 14-17 as unpatentable under 35 U.S.C. 103(a) over Shamblott [PNAS 95:13726-13731 (1998)] when taken with Sambrook et al [Molecular Cloning, Book 3, 1989]. The Examiner again asserts that the primordial germ cells (PGCs) of Shamblott are not considered totipotent, but are pluripotent, because they do not produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. Although the cells have the ability to colonize the germline, the cells also have the ability to differentiate to other cells. Thus, the Examiner states, the cells of Shamblott fulfill the limitations of the definition of "pluripotent". While Shamblott does not teach the transfection of the stem cells, Sambrook is noted as teaching methods of transfecting mammalian cells with any gene of interest. The Examiner takes the position that the combined teachings of Shamblott and Sambrook make it obvious for one of skill in the art at the time to use the Shamblott PGCs and transfect them with any DNA of interest, with a reasonable expectation of success.

Applicants again assert that the claimed pluripotent embryonic-like stem cells are distinguished from the Shamblott PGC cells and are not rendered obvious by the combination of the Shamblott and Sambrook references. The pluripotent embryonic stem cells are distinct from embryonic stem cells and primordial germ cells, particularly in that they are pluripotent and are not totipotent. Applicants again underscore that the claimed ELSCs when grown under inducing conditions as a population of isolated cells do not form gametes, as further evidenced by the

inventor's declaration previously submitted. Shamblott states in the introduction on page 13726:

> Embryonic stem (ES) cells are derived from the inner cell mass of preimplantation embryos and embryonic germ (EG) cells are derived from primordial germ cells (PGCs). Both ES and EG cells are pluripotent and demonstrate germ-line transmission in experimentally produced chimeras.

Applicants further point out that the claims have above been amended to more clearly and fully set out the characteristics of the PPELSCs and distinctions with other stem cells, including ES cells and PGCs. The claims as amended set out several aspects of distinction between the PPELSCs of Applicants and PGCs cells, including the cells of Shamblott et al. The instantly described and claimed cells are not derived from embryonic tissue and are not totipotent, as previously detailed and argued. In addition, while PGCs cells are recognized as spontaneously differentiating, forming disorganized and heterogenous gatherings of cells in culture (embryoid bodies - as described in Shamblott, including at page 13729), and forming teratomas (tumors) (as described in Shamblott, including at page 13726) in animals, the PPELSCs of applicants do not spontaneously differentiate, remaining quiescent in serum-free medium and in the absence of an induction agent, and also do not form tumors in an animal. The cells of the Shamblott et al reference are distinct from and do not teach or anticipate the PPELSC stem cells identified and claimed by Applicants. The Sambrook reference, teaching only methods of transfecting mammalian cells with a gene of interest, does not make the genetically modified PPELSCs obvious when combined with Shamblott.

The Examiner again rejects claims 14-17 under 35 U.S.C. 103(a) as being unpatentable over Thomson [Reference BR on Applicants' IDS filed 7/3/03, PNAS USA 92:7844-7848 (1995)] when taken with Sambrook [Molecular Cloning, Book 3, 1989]. The Examiner again asserts that the cells of Thomson are not considered totipotent, but are pluripotent, because they do not produce extra embryonic membranes, tissues, the embryo proper and all postembryonic tissues and organs. Again, the Examiner states that "furthermore, although pluripotent cells have the ability/capability to colonize the germline, pluripotent cells also have the ability to differentiate to other cells, as evidenced by the

production of chimeric animals". Applicants submit that the Examiner is factually incorrect. Pluripotent cells do NOT have the ability/capability to colonize the germline. Totipotent cells have the ability/capability to colonize the germline. ES cells are totipotent and CAN contribute to the germline. Applicants again assert that the claimed pluripotent embryonic-like stem cells are distinct and unobvious from the cells of Thomson, which are ES cells and can colonize the germline. Furthermore, PPELSCs are not made obvious by the combination of ES cells taught in Thomson with the transfection of mammalian cells taught by Sambrook. ES cells are totipotent and are capable of giving rise to all somatic lineages (ectodermal, endodermal and mesodermal) and can contribute to the germline, forming gametes. The pluripotent embryonic-like stem cells of the present invention are pluripotent and are capable of differentiation to somatic cells of any endodermal, ectodermal, mesodermal lineage, but are not totipotent. Applicants further point out that the claims have above been amended to more clearly and fully set out the characteristics of the PPELSCs and distinctions with other stem cells, including ES cells and PGCs. The claims as amended set out several aspects of distinction between the PPELSCs of Applicants and ES cells, including the cells of Thomson et al. The instantly described and claimed cells are not derived from embryonic tissue and are not totipotent, as previously detailed and argued. In addition, while ES cells are recognized as spontaneously differentiating, forming disorganized and heterogenous gatherings of cells in culture (embryoid bodies), and forming teratomas (tumors) in animals, the PPELSCs of applicants do not spontaneously differentiate, remaining quiescent in serum-free medium and in the absence of an induction agent, and also do not form tumors in an animal. The ES cells of the Thomson et al reference are distinct from and do not teach or anticipate the PPELSC stem cells identified and claimed by Applicants. The combination of Thomson and Sambrook does not make obvious the genetically engineered pluripotent embryonic-like stem cells as claimed by Applicants.

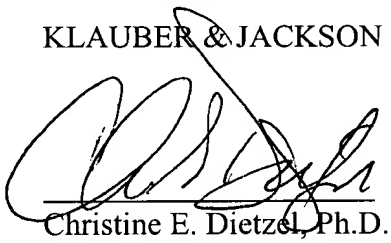
In view of the foregoing amendments and remarks, Applicants submit that the Examiner's 103 rejections are obviated and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Should the Examiner feel that further issues remain upon a review of this Response, he is invited to call the undersigned at the number listed below to effect their resolution. Early and favorable action on the claims is earnestly solicited.

No additional fees are believed to be necessitated by this response, however, in the event the U.S. Patent and Trademark office determines that claim fees, a further extension and/or other relief is required, applicant petitions for any required relief including extensions of time and claim fees and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 11-1053** referencing Docket no. 1304-1-019CIP.

Respectfully submitted,
KLAUBER & JACKSON



Christine E. Dietzel, Ph.D.
Agent for Applicant(s)
Registration No. 37,309

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack NJ 07601
Tel: (201) 487-5800